Complete Summary

GUIDELINE TITLE

Systemic therapy for advanced or recurrent endometrial cancer, and advanced or recurrent uterine papillary serous carcinoma.

BIBLIOGRAPHIC SOURCE(S)

Gynecology Cancer Disease Site Group. Gawlik C, Carey M, Faught W, Fung Kee Fung M, Chambers A. Systemic therapy for advanced or recurrent endometrial cancer, and advanced or recurrent uterine papillary serous carcinoma [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 Aug 17. 31 p. (Practice guideline report; no. 4-8). [53 references]

GUIDELINE STATUS

This is the current release of the guideline.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Advanced or recurrent endometrial cancer (excluding sarcomas and squamous cell carcinomas) or uterine papillary serous carcinoma

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Obstetrics and Gynecology
Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To evaluate the chemotherapeutic and hormonal therapy options for women with advanced or recurrent endometrial cancer (excluding sarcomas and squamous cell carcinomas)
- To evaluate the chemotherapeutic options for women with advanced or recurrent uterine papillary serous carcinoma

TARGET POPULATION

Adult patients diagnosed with advanced stage or recurrent endometrial cancer (excluding sarcomas and squamous cell carcinomas) or uterine papillary serous carcinoma.

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment

Chemotherapy Regimens

1. Doxorubicin/cisplatin versus doxorubicin/cisplatin/paclitaxel, doxorubicin alone, radiotherapy, carboplatin/paclitaxel, and doxorubicin/paclitaxel
2. Ifosfamide versus cyclophosphamide
3. Methotrexate/vinblastine/doxorubicin/cisplatin versus doxorubicin/cisplatin
4. Doxorubicin/cyclophosphamide versus doxorubicin alone
5. Doxorubicin/cyclophosphamide/cisplatin versus cisplatin alone
6. Doxorubicin versus cyclophosphamide

Chemotherapy Plus Hormonal Therapy

1. Cyclophosphamide/doxorubicin/5-fluorouracil/megestrol versus melphalan/5-fluorouracil/megestrol
2. Doxorubicin/cyclophosphamide/megestrol versus cyclophosphamide/doxorubicin/5-fluorouracil/megestrol

Hormonal Therapy

1. Megestrol versus megestrol/tamoxifen
2. Medroxyprogesterone acetate (200 mg/day versus 1,000 mg/day)
3. Medroxyprogesterone acetate versus tamoxifen
4. Gonadotrophin-releasing hormone and lutenizing hormone-releasing hormone analogs
5. Aromatase inhibitors
6. LY353381 (selective estrogen receptor modulator)

Systemic Therapy

1. Platinum plus paclitaxel
2. Paclitaxel alone
3. Cisplatin/doxorubicin/cyclophosphamide

Other Agents

1. Oral etoposide
2. Dactinomycin
3. Topotecan
4. Liposomal doxorubicin
5. Vinorelbine

MAJOR OUTCOMES CONSIDERED

- Median survival
- Tumour response (complete response, partial response, response rate)
- Quality of life
- Adverse events

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The MEDLINE (1966 to April 2004), CANCERLIT (1975 to October 2002), and Cochrane Library (2004, Issue 1) databases were searched using the Medical Subject Headings (MeSH) endometrial neoplasms, uterine neoplasms, and antineoplastic agents, and the following text words: endometrium, endometrial, serous, uterus, uterine, cancer, carcinoma, chemotherapy, hormone(s), hormonal. Search terms related to study design or publication type included systematic review, clinical trial, meta-analysis, controlled clinical trials, clinical trials/phase II, clinical trials/phase III, multicentre studies, and randomized controlled trials (MeSH). Proceedings of the 1997 to 2003 meetings of the American Society of Clinical Oncology (ASCO) and reference lists of papers and review articles were scanned for additional citations. The Canadian Medical Association Infobase (www.cma.ca/cma/common/start.do?lang=2) and the National Guidelines

Clearinghouse (www.guideline.gov) Web sites were searched for existing evidence-based practice guidelines.

Inclusion Criteria

Evidence-based clinical practice guidelines or systematic reviews regarding systemic therapy for advanced disease from other guideline-development groups were eligible for inclusion.

To address the question regarding the chemotherapeutic and hormonal therapy options for women with advanced or recurrent endometrial cancer, full articles or abstracts were selected for inclusion if they met the following criteria:

1. Randomized controlled trials (RCT) or meta-analyses comparing regimens of systemic chemotherapy or hormonal therapy to the standard treatment for advanced or recurrent endometrial cancer reporting at least one of the following outcomes: survival, quality of life, response rate, or toxicity
2. RCTs that reported on heterogeneous populations (e.g., included women with a range of disease stages) were eligible if results were given separately for the group with advanced or recurrent endometrial cancer.
3. When RCTs were not available, phase II trials of chemotherapy and hormonal therapy agents were included.

To address the question regarding the chemotherapeutic options for women with advanced or recurrent uterine papillary serous carcinoma (UPSC), full articles or abstracts were selected for inclusion if they met the following criteria:

1. RCTs comparing systemic therapy regimens that included women with stage IIIc or IV uterine papillary serous carcinoma with measurable or evaluable disease at the start of systemic therapy, and reported at least one of the following outcomes: survival, quality of life, response rate, or toxicity
2. When RCTs were not available, phase II trials of chemotherapy agents were included.

Exclusion Criteria

1. Non-English language publications were excluded.
2. Studies evaluating the role of radiotherapy, administered with chemotherapy or hormonal therapy, were excluded.

NUMBER OF SOURCE DOCUMENTS

17 randomized controlled trials, 26 phase II studies, and 4 non-comparative studies were reviewed.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The Gynecology Cancer Disease Site Group (DSG) identified 17 randomized controlled trials (RCTs) that compared various chemotherapy regimens for the treatment of advanced or recurrent endometrial cancer, including abstracts and randomized phase II trials. The results of randomized controlled trials could not be pooled because of the differences among the studies in terms of:

1. The number of advanced versus recurrent cases. Advanced cases actually have a poorer prognosis with a shorter expected survival than most patients presenting with recurrence.
2. The greater proportion of patients previously treated with radiation therapy and documentation with respect to the site of recurrence (either in or out of the radiated field). Patients with disease in the radiated field are known to have lower response rates to systemic chemotherapy than patients with disease outside the field.
3. The inclusion or exclusion of adverse histologic subtypes. Trials differed with respect to the inclusion or exclusion of patients with adverse histologic subtypes. It was only within the last three to five years that the Gynecologic Oncology Group (GOG) decided to separate patients with serous carcinomas as a distinct entity in subsequent Gynecologic Oncology Group studies.
4. The inclusion criteria concerning previous systemic therapy. There were marked differences among studies with respect to the number of prior chemo-hormonal regimens administered to patients.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 81 practitioners in Ontario (11 gynecologists, 39 medical oncologists, 18 radiation oncologists, and 13 surgeons). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations above should be approved as a practice guideline. Written comments were invited. The practitioner feedback survey was mailed out on October 27, 2003. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Gynecology Cancer Disease Site Group (DSG) reviewed the results of the survey.

The practice guideline report was circulated to members of the Practice Guidelines Coordinating Committee (PGCC) for review and approval. Seven of 14 members of the PGCC returned ballots. Four PGCC members approved the practice guideline report as written, and one member approved the report with a minor editorial change to the recommendations required. One member approved the report conditional on the Gynecology DSG clarifying the recommendations. One PGCC member did not approve the report because the member was concerned that the guideline placed too much emphasis on the abstract by Fleming et al comparing doxorubicin/cisplatin to doxorubicin/paclitaxel/cisplatin. The PGCC member thought that the Gynecology DSG should wait until the randomized controlled trial (RCT) was reported in a full publication before making recommendations based on the trial.

Final approval of the practice guideline report is obtained from the Practice Guidelines Coordinating Committee.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

For women with advanced or recurrent endometrial cancer:

- Combination chemotherapy is favoured over single agent chemotherapy because of higher response rates.
- Paclitaxel in combination with cisplatin/doxorubicin chemotherapy improves both response rate and median survival; however, the use of this three-drug combination is associated with increased toxicity.
- Hormonal therapy may be a therapeutic option for those patients with minimal symptoms or non-life threatening advanced or recurrent endometrial cancer.

For women with uterine papillary serous carcinoma:

- Evidence supporting or refuting various chemotherapy regimens for uterine papillary serous carcinoma is limited.
- Patients should be encouraged to participate in randomized trials.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized controlled trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved understanding of the chemotherapeutic and hormonal therapy options for women with advanced or recurrent endometrial cancer or recurrent uterine papillary serous carcinoma

POTENTIAL HARMS

- Neuropathy, hematological, and gastrointestinal toxicities were the most common adverse effects reported; toxicity increased in incidence with the increase in the number of agents used.
- Hormonal agents were well tolerated: adverse effects were reported at less than 5%.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The decision to use the three-drug combination, consisting of cisplatin/doxorubicin/paclitaxel, should be made in consultation with the patient. Consideration needs to be given to both the greater toxicity and the three-month increase in median survival time achieved with the three-drug combination in comparison with the two-drug doxorubicin/cisplatin regimen.
- For uterine papillary serous carcinoma treatment (UPSC), the most studied regimen is a paclitaxel/platinum combination. The addition of paclitaxel in small, non-comparative studies is associated with improved response rates and survival compared to non-platinum containing regimens.
- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the practice guideline is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Aug 17

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Gynecology Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Gynecology Cancer Disease Site Group (DSG) disclosed potential conflict of interest information.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Systemic therapy for advanced or recurrent endometrial cancer, and advanced or recurrent uterine papillary serous carcinoma. Summary. Toronto (ON): Cancer Care Ontario. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on October 6, 2004. The information was verified by the guideline developer on October 20, 2004.

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Date Modified: 9/25/2006